



## SEQUENCE LISTING

<110> TUSZYNSKI, MARK  
BLESCH, ARMIN

<120> MUTANT PRO-NEUROTROPHIN WITH IMPROVED ACTIVITY

<130> 041673/2045

<140> 09/788,188

<141> 2001-02-16

<160> 16

<170> PatentIn Ver. 2.1

<210> 1

<211> 241

<212> PRT

<213> Homo sapiens

<400> 1

Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile  
1 5 10 15

Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile  
20 25 30

Pro Gln Val His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu  
35 40 45

Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala  
50 55 60

Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg  
65 70 75 80

Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu  
85 90 95

Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro  
100 105 110

Phe Asn Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe  
115 120 125

His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly  
130 135 140

Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu  
145 150 155 160

Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu  
165 170 175

Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile  
180 185 190

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Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val  
 195 200 205

Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg  
 210 215 220

Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg  
 225 230 235 240

Ala

<210> 2  
 <211> 241  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Mutant NGF  
 pro-neurotrophin

<400> 2  
 Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile  
 1 5 10 15

Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile  
 20 25 30

Pro Gln Val His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu  
 35 40 45

Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala  
 50 55 60

Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg  
 65 70 75 80

Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu  
 85 90 95

Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro  
 100 105 110

Phe Ser Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe  
 115 120 125

His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly  
 130 135 140

Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu  
 145 150 155 160

Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu  
 165 170 175

Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile  
 180 185 190

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Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val  
 195 200 205  
 Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg  
 210 215 220  
 Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg  
 225 230 235 240  
 Ala

<210> 3  
 <211> 247  
 <212> PRT  
 <213> Homo sapiens

<400> 3  
 Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met  
 1 5 10 15  
 Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu  
 20 25 30  
 Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly  
 35 40 45  
 Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu  
 50 55 60  
 His Val Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn  
 65 70 75 80  
 Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu  
 85 90 95  
 Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu  
 100 105 110  
 Tyr Lys Asn Tyr Leu Asp Ala Ala Asn Met Ser Met Arg Val Arg Arg  
 115 120 125  
 His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile  
 130 135 140  
 Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser  
 145 150 155 160  
 Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln  
 165 170 175  
 Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr  
 180 185 190  
 Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys  
 195 200 205

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Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys  
210 215 220

Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr  
225 230 235 240

Leu Thr Ile Lys Arg Gly Arg  
245

<210> 4

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Mutant BDNF  
pro-neurotrophin

<400> 4

Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met  
1 5 10 15

Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu  
20 25 30

Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly  
35 40 45

Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu  
50 55 60

His Val Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn  
65 70 75 80

Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu  
85 90 95

Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu  
100 105 110

Tyr Lys Asn Tyr Leu Asp Ala Ala Ser Met Ser Met Arg Val Arg Arg  
115 120 125

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile  
130 135 140

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser  
145 150 155 160

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln  
165 170 175

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr  
180 185 190

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Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys  
 195 200 205  
 Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys  
 210 215 220  
 Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr  
 225 230 235 240  
 Leu Thr Ile Lys Arg Gly Arg  
 245

<210> 5  
 <211> 257  
 <212> PRT  
 <213> Homo sapiens

<400> 5  
 Met Ser Ile Leu Phe Tyr Val Ile Phe Leu Ala Tyr Leu Arg Gly Ile  
 1 5 10 15  
 Gln Gly Asn Asn Met Asp Gln Arg Ser Leu Pro Glu Asp Ser Leu Asn  
 20 25 30  
 Ser Leu Ile Ile Lys Leu Ile Gln Ala Asp Ile Leu Lys Asn Lys Leu  
 35 40 45  
 Ser Lys Gln Met Val Asp Val Lys Glu Asn Tyr Gln Ser Thr Leu Pro  
 50 55 60  
 Lys Ala Glu Ala Pro Arg Glu Pro Glu Arg Gly Gly Pro Ala Lys Ser  
 65 70 75 80  
 Ala Phe Gln Pro Val Ile Ala Met Asp Thr Glu Leu Leu Arg Gln Gln  
 85 90 95  
 Arg Arg Tyr Asn Ser Pro Arg Val Leu Leu Ser Asp Ser Thr Pro Leu  
 100 105 110  
 Glu Pro Pro Pro Leu Tyr Leu Met Glu Asp Tyr Val Gly Ser Pro Val  
 115 120 125  
 Val Ala Asn Arg Thr Ser Arg Arg Lys Arg Tyr Ala Glu His Lys Ser  
 130 135 140  
 His Arg Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr  
 145 150 155 160  
 Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu  
 165 170 175  
 Gly Glu Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu  
 180 185 190  
 Thr Arg Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile  
 195 200 205

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Asp Asp Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val  
 210 215 220  
 Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile  
 225 230 235 240  
 Arg Ile Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg  
 245 250 255

Thr

<210> 6  
 <211> 257  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Mutant NGF  
 pro-neurotrophin

<400> 6  
 Met Ser Ile Leu Phe Tyr Val Ile Phe Leu Ala Tyr Leu Arg Gly Ile  
 1 5 10 15  
 Gln Gly Asn Asn Met Asp Gln Arg Ser Leu Pro Glu Asp Ser Leu Asn  
 20 25 30  
 Ser Leu Ile Ile Lys Leu Ile Gln Ala Asp Ile Leu Lys Asn Lys Leu  
 35 40 45  
 Ser Lys Gln Met Val Asp Val Lys Glu Asn Tyr Gln Ser Thr Leu Pro  
 50 55 60  
 Lys Ala Glu Ala Pro Arg Glu Pro Glu Arg Gly Gly Pro Ala Lys Ser  
 65 70 75 80  
 Ala Phe Gln Pro Val Ile Ala Met Asp Thr Glu Leu Leu Arg Gln Gln  
 85 90 95  
 Arg Arg Tyr Asn Ser Pro Arg Val Leu Leu Ser Asp Ser Thr Pro Leu  
 100 105 110  
 Glu Pro Pro Pro Leu Tyr Leu Met Glu Asp Tyr Val Gly Ser Pro Val  
 115 120 125  
 Val Ala Ser Arg Thr Ser Arg Arg Lys Arg Tyr Ala Glu His Lys Ser  
 130 135 140  
 His Arg Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr  
 145 150 155 160  
 Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu  
 165 170 175  
 Gly Glu Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu  
 180 185 190

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Thr Arg Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile  
 195 200 205

Asp Asp Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val  
 210 215 220

Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile  
 225 230 235 240

Arg Ile Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg  
 245 250 255

Thr

<210> 7  
 <211> 210  
 <212> PRT  
 <213> Homo sapiens

<400> 7  
 Met Leu Pro Leu Pro Ser Cys Ser Leu Pro Ile Leu Leu Leu Phe Leu  
 1 5 10 15

Leu Pro Ser Val Pro Ile Glu Ser Gln Pro Pro Pro Ser Thr Leu Pro  
 20 25 30

Pro Phe Leu Ala Pro Glu Trp Asp Leu Leu Ser Pro Arg Val Val Leu  
 35 40 45

Ser Arg Gly Ala Pro Ala Gly Pro Pro Leu Leu Phe Leu Leu Glu Ala  
 50 55 60

Gly Ala Phe Arg Glu Ser Ala Gly Ala Pro Ala Asn Arg Ser Arg Arg  
 65 70 75 80

Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val  
 85 90 95

Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp  
 100 105 110

Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly  
 115 120 125

Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp  
 130 135 140

Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Cys Arg Gly  
 145 150 155 160

Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr  
 165 170 175

Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp  
 180 185 190

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Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly  
 195 200 205

Arg Ala  
 210

<210> 8

<211> 210

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Mutant NT-4/5  
 pro-neurotrophin

<400> 8

Met Leu Pro Leu Pro Ser Cys Ser Leu Pro Ile Leu Leu Leu Phe Leu  
 1 5 10 15

Leu Pro Ser Val Pro Ile Glu Ser Gln Pro Pro Pro Ser Thr Leu Pro  
 20 25 30

Pro Phe Leu Ala Pro Glu Trp Asp Leu Leu Ser Pro Arg Val Val Leu  
 35 40 45

Ser Arg Gly Ala Pro Ala Gly Pro Pro Leu Leu Phe Leu Leu Glu Ala  
 50 55 60

Gly Ala Phe Arg Glu Ser Ala Gly Ala Pro Ala Ser Arg Ser Arg Arg  
 65 70 75 80

Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val  
 85 90 95

Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp  
 100 105 110

Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly  
 115 120 125

Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp  
 130 135 140

Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Gly Cys Arg Gly  
 145 150 155 160

Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr  
 165 170 175

Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp  
 180 185 190

Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly  
 195 200 205

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Arg Ala  
210

<210> 9  
<211> 726  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Recombinant  
coding sequence for NGF

<400> 9  
atgtccatgt tgttctacac tctgatcaca gcttttctga tcggcataca ggcggaacca 60  
cactcagaga gcaatgtccc tgcaggacac accatcccc aagtccactg gactaaactt 120  
cagcattccc ttgacactgc ctttcgcaga gcccgagcg ccccggcagc ggcgatagct 180  
gcacgcgtgg cggggcagac ccgcaacatt actgtggacc ccaggctgtt taaaaagcgg 240  
cgactccgtt caccctcgtgt gctgttttagc acccagcctc cccgtgaagc tgcagacact 300  
caggatctgg acttcgaggt cgggtgtgtc gcccccttca acaggactca caggagcaag 360  
cggtcacatc cccatcccat cttccacagg ggcgaattct cggtgtgtga cagtgtcagc 420  
gtgtgggttg gggataagac caccgccaca gacatcaagg gcaaggaggt gatgggtgtg 480  
ggagaggtga acattaacaa cagtgtattc aaacagtact tttttgagac caagtgccgg 540  
gacccaaatc ccgttgacag cgggtgccgg ggcattgact caaagcactg gaactcatat 600  
tgtaccacga ctcacacctt tgtcaaggcg ctgaccatgg atggcaagca ggctgcctgg 660  
cggtttatcc ggatagatac ggctgtgtg tgtgtgtcga gcaggaaggc tgtgagaaga 720  
gcctga 726

<210> 10  
<211> 676  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Recombinant  
coding sequence for NT-3 precursor

<220>  
<221> modified\_base  
<222> (525)  
<223> a, t, c, g, other or unknown

<220>  
<221> modified\_base  
<222> (606)  
<223> a, t, c, g, other or unknown

<220>  
<221> modified\_base  
<222> (619)..(620)  
<223> a, t, c, g, other or unknown

<220>  
<221> modified\_base  
<222> (632)  
<223> a, t, c, g, other or unknown

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<400> 12						
atgctccctc	tccctcatg	ctccctcccc	atcctcctcc	ttttctctct	ccccagtgtg	60
ccaattgagt	cccaaccccc	accctcaaca	ttgccccctt	ttctggcccc	tgagtgggac	120
cttctctccc	cccgagtagt	cctgtctagg	ggtgccccctg	ctgggcccccc	tctgctcttc	180
ctgctggagg	ctggggcctt	tcgggagtc	gcaggtgccc	cggccaaccg	cagccggcgt	240
ggggtgagcg	aaactgcacc	agcgagtcgt	cggggtgagc	tggctgtgtg	cgatgcagtc	300
agtggctagg	tgacagaccg	ccgggaccgt	gtggacttgc	gtgggcgcga	ggtggagggtg	360
ttgggcyagg	tgctgtcagc	tggcggcagt	ccctcccgcc	agtacttctt	tgaaacccgc	420
tgcaaggctg	ataacgctga	ggaagggtggc	ccgggggcag	gtggaggggg	ctgccgggga	480

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<210> 13
<211> 465
<212> DNA
<213> Artificial Sequence
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400 13						
tttttatttt	ttttaacttt	ttatgttttc	agttcttggc	aacggcaaca	aaccacaaca	60
ttatcaagga	atgtaatgca	gactttttta	gttggtgcga	aatgactggt	tcccttctgg	120
tcatggacat	gtccaataaa	tagattgtag	aaccactgta	ctgtataaac	ttcatttata	180
catgcagttc	ataaaattat	ttttttctta	actgaataat	ttaccctggg	atgtatatat	240
tacaaataga	taatttttgt	ctcaatataa	tctaattctat	acaacataaa	tccactatct	300
tcccccttta	atggtcaatg	tacatacata	agaagtgtct	atccttatga	atcgccagcc	360
aattctcttt	ttgctattcca	tggtaagggc	cgcacgtac	gactgggtag	ttcggcactg	420
ggagttccaa	tgccttttgt	ctatgccctt	gcagccttct	tttgtt		465

<220>  
<223> Description of Artificial Sequence: Primer

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<210> 15
<211> 30
<212> DNA
<213> Artificial Sequence
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<400> 15  
tgtggatcct caggctcttc tcacagcctt 30

<220>  
<223> Description of Artificial Sequence: Recombinant  
DNA

&lt;400&gt; 16

atgtccatgt	tgttctacac	tctgatcaca	gcttttctga	tgggcataca	ggcggaaacca	60
cactcagaga	gcaatgtccc	tgcaggacac	accatcccc	aagtccactg	gactaaactt	120
cagcattccc	ttgacactgc	ccttcgcaga	gcccgcagcg	ccccggcagc	ggcgatagct	180
gcacgcgtgg	cggggcagac	ccgcaacatt	actgtggacc	ccaggctgtt	taaaaagcgg	240
cgactccgtt	caccccgtgt	gctgttttagc	accagcctc	cccgtgaagc	tgcagacact	300
caggatctgg	acttcgaggt	cgggtggtgct	gcccccttca	gcaggactca	caggagcaag	360
cggtcacat	cccatcccat	cttccacagg	ggcgaattct	cgggtgtgtga	cagtgtcagc	420
gtgtgggttg	gggataagac	caccgccaca	gacatcaagg	gcaaggaggt	gatggtgttg	480
ggagaggtga	acattaacaa	cagtgtattc	aaacagtact	tttttgagac	caagtgccgg	540
gacccaaatc	ccgttgacag	cgggtgccgg	ggcattgact	caaagcactg	gaactcatat	600
tgtaccacga	ctcacacctt	tgtcaaggcg	ctgaccatgg	atggcaagca	ggctgcctgg	660
cggtttatcc	ggatagatac	ggcctgtgtg	tgtgtgctca	gcaggaaggc	tgtgagaaga	720
gcctga						726

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